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VENTRICULAR ARRHYTHMIAS: WHAT WORRIES ME IN HORSES?

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Introduction

A wide variety of cardiac arrhythmias have been recognized in horses, some that are physiologic and others that are potentially dangerous. These arrhythmias can develop as isolated electrical disorders or secondary to other etiological factors.

Of principal concern to the equine clinician are the hemodynamic consequences of arrhythmias (hypotension, low cardiac output, poor peripheral perfusion) and the potential for further electrical destabilization (malignant, potentially fatal arrhythmias). Generally, ventricular arrhythmias are of greater concern in regard to performance capacity and safety of horses compared to supraventricular arrhythmias.

Defining safety risks

Defining the safety risks to the horse and to the rider or driver is critical in cases of ventricular ectopy. Generally, premature ventricular complexes (PVCs) are considered abnormal in the horse. However, isolated PVCs may be more common than recognized from routine ECG studies, even in apparently healthy horses. Not all ectopic ventricular rhythms are considered equally dangerous and the complexity of ventricular arrhythmias is presumed to relate to the risk of hypotension, weakness, collapse and sudden cardiac death (SCD) because of ventricular fibrillation. However, risk stratification for ventricular arrhythmias is imperfect, particularly in horses with isolated PVCs at rest and/or during exercise.

In the absence of clear evidence, recommendations should be biased toward safety, as opposed to maintaining athletic activity. Certainly, a history of collapse or co-existence of important structural heart disease (and cardiomegaly) raises great concern in a horse with PVCs. However, in the absence of obvious clinical signs or of serious structural heart disease, the risk of ventricular ectopy is usually defined by electrocardiographic characteristics, accepting the limitations of this analysis. This assessment includes timing, rate and morphology of the ectopic activity.

As a general rule, ventricular arrhythmias should be considered complex or “malignant” and potentially life threatening, if they are characterized by one or more of the following criteria:

- Repetitive or sustained ectopic rhythms
- Very rapid ventricular rate (exceeding 120 beats/min at rest)
- Multiform or polymorphic QRS morphology (including torsades de pointes)
- Short coupling interval with R-on-T phenomenon (i.e., PVCs occurring on the peak of the preceding T wave)

Complex ventricular arrhythmias can induce hemodynamic impairment resulting in clinical evidence of low cardiac output (e.g., weakness, stumbling, pale mucous membranes, prolonged CRT, syncope) and hypotension. Electrical instability is a particular concern in malignant ventricular arrhythmias and can cause ventricular tachycardia to progress into ventricular flutter or ventricular fibrillation. These commonly represent terminal events.

Many cases with ventricular arrhythmia can be managed by treating the underlying disease and rest. Repeated or continuous ECG monitoring (to document progression of disease or resolution of arrhythmia) is recommended. Complex, “malignant” ventricular arrhythmias should be more aggressively managed by additional use of antiarrhythmic drugs.

Ventricular arrhythmias during exercise

A wide range of ventricular arrhythmias has been reported during and immediately following intense exercise in normally performing horses and horses presented for poor performance. However, the clinical relevance of most of these arrhythmias and their relationship to poor performance and sudden cardiac death is not well defined. Generally, occasional monomorphic PVCs overdriven with exercise or only detected in the immediate post-exercise period are not considered a cause for poor performance. Conversely, PVCs occurring during exercise are considered a cause for concern.

Generally, the criteria for complexity and “malignancy” of ventricular arrhythmias listed above also apply during exercise. However, diagnosing ventricular arrhythmias during exercise is often difficult, since telemetric ECG recordings are affected by motion artefacts. Furthermore, prematurity of ectopic beats is difficult to detect at high heart rates, even when RR intervals are measured using ECG calipers. On modern digital ECG systems, this can be achieved by automated RR analyses, but algorithms are imperfect and prone to error and usually require visual validation by the operator. Also, the distinction between (pathologic) prematurity and (physiologic) heart rate variability can be difficult. The current knowledge indicates that sudden shortening of the RR interval by more than 5-7% during trot and canter phases indicates prematurity, whereas variation of less than 4-5% likely indicates normal heart rate variability. However, exact criteria are lacking to date. The traditional criteria to differentiate ventricular from supraventricular arrhythmias (association with P wave, shape and orientation of QRS complex and T wave) are difficult to apply to exercising ECGs and at high heart rates, and often times premature ectopic beats cannot be unambiguously classified as

supraventricular and ventricular, respectively. Finally, variability over time of the frequency and "malignancy" of ventricular arrhythmias in horses is currently unknown. Also, the influence of different types of exercise (e.g., lunging vs. treadmill exercise vs. ridden exercise) on ventricular arrhythmias is not well defined.

Ventricular arrhythmias associated with aortic regurgitation

Aortic regurgitation (AR) is a common (and often incidental) finding in older horses. It is often mild and associated with a normal life expectancy and performance capacity. However, sudden cardiac death associated with fatal ventricular arrhythmias has been observed and is a concern in horses with moderate to severe AR and can occur without poor performance or CHF.

Therefore, all horses with a heart murmur consistent with AR should be evaluated carefully. Clinically, bounding or hyperkinetic arterial pulses and a pulse pressure of > 60 mm Hg (measured by non-invasive blood pressure recordings) suggest hemodynamically relevant AR with LV volume overload and increased likelihood of progression. Echocardiography is recommended to identify the most likely etiology and further assess disease severity. A continuous 24h-Holter ECG and an exercising ECG are recommended when moderate to severe AR and/or performance issues are evident. Analyses should be focused on identifying PVCs at rest and during exercise and appropriateness of the exercising heart rate.

Owing to a risk for SCD, horses with moderate to severe AR should not be ridden by a child or used as a lesson horse or in a high-risk sport. Affected horses should initially be re-examined twice yearly (including echocardiography and ECG exercise test) and at least annually thereafter if progression has been minimal. Heart rate and rhythm should be monitored on a regular basis; an increased resting HR or an irregularly irregular rhythm suggesting atrial fibrillation or PVCs indicate progression of disease. The detection of exercise-induced ventricular arrhythmias is considered an important negative prognostic indicator. Horses with AR and PVCs during exercise are considered less safe to ride than their age-matched peers.

Ventricular arrhythmias associated with atrial fibrillation

Atrial fibrillation (AF) is the most common arrhythmia affecting performance. Although uncommon, collapse during exercise has been reported with AF. Safety is a particular concern with persistent AF when the average maximal heart rate (HR) during exercise at an intensity that is at or slightly exceeding the horse's normal activities is greater than 220/minute. Additionally, ventricular ectopy during exercise or during sympathetic stimulation is not unfrequently observed in association with AF and indicates a possible risk for SCD, particularly when short R-R intervals or R-on-T phenomenon are present. AF associated with exercise-induced ventricular arrhythmias resulting in SCD has been documented by telemetric ECG in at least one horse.

Exercise testing with stress ECG should always be conducted when a horse is used for performance. Cardioversion of persistent AF is strongly recommended for all horses used for athletic activities when the exercising HR during sustained maximal exercise exceeds 220 beats /minute or concurrent ventricular arrhythmias are detected during exercise or with sympathetic stimulation. Ventricular arrhythmias usually resolve after cardioversion.

When cardioversion is not an option or could not be attained, horses with persistent AF should only be used by informed adult riders and limited to an exercise level considered relatively safe based on exercising ECG. The use of a HR monitor might be useful to track heart rate during exercise and modify the rigor of the work performed. Horses with persistent AF and exceedingly high exercising HR or exercise-induce ventricular ectopy with short R-R intervals or R-on-T phenomenon should be retired for safety reasons.

Cardioversion of AF should only be performed in a controlled setting with continuous (ECG) monitoring, regardless of the treatment method, since all treatments can be associated with adverse events, including (but not limited to) ventricular arrhythmias.

Quinidine sulfate is still the mainstay of pharmacological cardioversion of AF. Potential risks of quinidine cardioversion include rapid ventricular response to AF and complex ventricular ectopy owing to the potential for QT prolongation, proarrhythmia and polymorphic ventricular tachycardia. Such events sometimes necessitate discontinuation of therapy or co-administration of other drugs to control the ventricular response rate or treat ventricular arrhythmias.

In horses with AF and elevated resting heart rate or with sustained (supraventricular) tachycardia during quinidine treatment, digoxin is commonly used for ventricular rate control. Due to the variable pharmacokinetics and the narrow therapeutic window, therapeutic drug monitoring, individualized selection of a digoxin dosage regimen, and close monitoring of the clinical response is advisable. Digoxin can result in supraventricular and ventricular arrhythmias (bigeminy). Factors predisposing to digitalis toxicity include advanced heart disease, atrial fibrillation, impaired renal function, hypokalemia, hypomagnesemia, hypercalcemia, and hypoproteinemia. Quinidine decreases renal clearance and increases circulating blood digoxin concentrations, while phenylbutazone competes with protein binding sites and increases the free digoxin fraction.

Other antiarrhythmic drugs, including amiodarone, flecainide and propafenone, have been used in horses with AF but are not currently recommended for treatment because of lack of efficacy and/or high risk of severe tachycardia and potentially fatal ventricular arrhythmias.

Transvenous electrical cardioversion (TVEC) is considered equivalent or superior to quinidine cardioversion in regard to short-term success of cardioversion, although studies directly comparing the two methods are lacking. In some institutions, TVEC is

currently the first-line treatment for AF. The procedure should be performed by experienced operators using specialized equipment and involves a timed shock delivery on the R-wave. The risks of TVEC include general anesthesia or rarely development of a fatal ventricular arrhythmia. The latter is of particular concern if the electrical shock is inadvertently delivered to the T wave, representing the vulnerable period for induction of malignant ventricular arrhythmias.

Sotalol may be used for maintenance of sinus rhythm after successful cardioversion of atrial fibrillation and for chronic treatment of supraventricular and ventricular arrhythmias. Although not well described in the current literature, preliminary studies and clinical experience indicate that orally administered sotalol is well tolerated in horses and is not associated with increased risk of ventricular arrhythmias at doses up to 2-3 mg/kg PO q12h. However, since QT prolongation and proarrhythmic effects are a concern, monitoring of QT interval is recommended.

Ventricular arrhythmias associated with systemic disease

Ventricular arrhythmias can be found in horses with a variety of medical and surgical disorders and are particularly common in horses with gastrointestinal disease. Their etiology is often undefined and likely multifactorial. Factors favoring the development of ventricular arrhythmias include electrolyte imbalances (e.g., hypokalemia, hypomagnesemia), acid-base disturbances, hypoxemia; metabolic and endocrine disorders; systemic inflammation, endotoxemia, sepsis, and fever; hypotension, hemorrhage, anemia, and ischemia; autonomic influences (i.e., high sympathetic or parasympathetic tone or autonomic imbalance); toxicosis/envenomation; and a variety of drugs (including antiarrhythmics, catecholamines, alpha-2 agonists, and anesthetics). Assessment of the overall clinical picture is important, since arrhythmias often resolve with correction of the underlying problem.

Ventricular ectopy observed with systemic disease encompasses the entire range from single, innocuous PVCs to malignant ventricular arrhythmias with tachycardia, multiform QRS conformation and R-on-T phenomenon, potentially triggering fatal ventricular events.

Accelerated idioventricular rhythms (AIVR, also termed slow ventricular tachycardias) are common in horses with systemic disease. They are usually well-tolerated, tend to be monomorphic, start with a relatively long coupling interval, and become established at relatively slow ventricular rates that are equal to or slightly above the sinoatrial rate (50-80/min at rest). AIVRs may easily be misdiagnosed as sinus tachycardia on auscultation or palpation of peripheral pulses, since these rhythms are often quite regular. Persistent, unexplained mild to moderate tachycardia should therefore prompt an ECG examination to ascertain a correct rhythm diagnosis. This said, accelerated idioventricular rhythms generally are of little clinical (electrophysiologic and hemodynamic) relevance and usually resolve spontaneously with appropriate treatment of potential underlying conditions. Electrolyte supplementation (potassium, magnesium) and correction of fluid deficits and acid-base disturbances may be beneficial. Lidocaine is sometimes administered as an intraoperative adjunct to general anesthesia or used as an analgesic and prokinetic drug in the management of post-operative ileus; in these situations, its antiarrhythmic effects may provide some additional preventive or therapeutic benefits.

More malignant ventricular arrhythmias may require immediate antiarrhythmic treatment in addition to management of the underlying disease and potential pro-arrhythmic factors.

Ventricular arrhythmias associated with long QT interval

The upper limits for the QT interval at resting heart rates are approximately 600 ms in adult horses and 350–400 ms in foals. However, the QT interval shortens at higher heart rates and strongly depends on changes in autonomic tone. A variety of population-based or individual-based methods have been used in other species to correct for heart rate-related changes. Although some data are available for horses, correction formulas cannot be uniformly used for different populations or easily applied to individual horses. The diagnosis of QT prolongation in horses is further complicated by the commonly encountered difficulties to accurately detect the end of the T wave.

Congenital (due to ion channel mutations) or acquired (due to drug effects on repolarizing currents) long QT syndrome (LQTS) associated with life-threatening cardiac arrhythmias and sudden death has not been well documented in horses. However, repolarizing currents in horses are similar to those in other species, and it has been suggested that horses may be at risk for acquired LQTS. Many drugs that potentially prolong cardiac repolarization in other species have also been used in horses, including quinidine, procainamide, flecainide, amiodarone, sotalol, cisapride, metoclopramide, erythromycin, clarithromycin, fluconazole, trimethoprim-sulfamethoxazole, sevoflurane, and isoflurane. Quinidine-induced torsades de pointes, potentially related to drug-induced QT prolongation, have been reported in horses. The slow resting heart rate and the hypokalemia commonly associated with gastrointestinal disease in horses theoretically enhance the risk of drug-induced arrhythmias. It therefore seems advisable to consider potential proarrhythmic effects when QT-prolonging drugs are administered to horses at risk.

Prognosis

The prognosis for horses with ventricular arrhythmias is usually favorable for infrequent, single ectopic beats in the absence of other signs of significant cardiac disease, or for arrhythmias which can be attributed to a treatable underlying non-cardiac disease. The prognosis for sustained ventricular tachycardia is usually guarded, particularly if there is evidence of significant structural heart disease or congestive heart failure. The prognosis for multiform ventricular tachycardia or torsades de pointes is usually poor.

Recommendations for PVCs and VT according to the 2014 ACVIM/ECEIM Consensus Statement on Management of Equine Athletes with Cardiovascular Abnormalities

- Underlying causes should be sought and managed if possible. Assessment of the overall clinical picture is important because ventricular arrhythmias (VA) can be associated with medical or surgical disorders and often resolve with correction of the underlying problem.
    - A clinical laboratory profile, including cardiac troponin I (cTnI) should be obtained from all horses.
    - While an echocardiogram may be valuable in any horse with VA, this test is specifically recommended for horses with VT or complex VA; when VA is recurrent or persistent; or when VA is identified in the clinical settings of poor performance, a pathologic cardiac murmur, or a significantly elevated cTnI. The echocardiogram should include imaging for abnormal myocardial echo texture, thickness, or scar, and exclusion of dissecting aortic aneurysm or aorto-cardiac fistula. Left ventricular dilation may be secondary to tachycardia-induced cardiomyopathy or ventricular dyssynchrony. In horses with sustained VT the echocardiogram should be repeated once the horse has returned to NSR.
    - A continuous 24-hour ECG should also be obtained to more completely evaluate the VA as they are often intermittent.
    - Further work-up of a horse with PVCs or AIVR, in the absence of underlying systemic disease, should include an exercising ECG. Horses with severe VA should not be exercise tested.
- Horses with occasional PVCs, with sustained AIVR that is overdriven by exercise or multiple PVCs during exercise may be used with caution by an informed adult rider. Owing to ongoing concerns about underlying myocardial or electrical disease and increased risks of exercise associated collapse and SCD; these horses should not be used by a child rider or as a lesson horse.
- Horses with sustained monomorphic VT should be rested and treated. NSR should be present for at least 4 weeks before re-evaluation is performed. A continuous 24-hour ECG is indicated prior to returning the horse to work. If normal, an exercising ECG should be performed, followed by another exercising ECG once the horse has returned to full work. Horses affected by a single episode generally have a favorable prognosis, but on occasion monomorphic VT can recur.
- Horses with symptomatic or complex VA should be rested and treated. Follow-up examinations are similar as for horses with sustained monomorphic VT although the safety of these horses remains uncertain. These horses should only be ridden by an informed adult rider.
- Rigorous athletic work is not recommended for horses that showed VA in the setting of moderate or severe structural heart disease, including focal myocardial fibrosis and moderate to severe AR. These horses should only be used by an informed adult rider due to the risk of possible recurrence of VT. These horses are not safe for use by a child rider or as a lesson horse.
- For horses with a history of VT that remain in work follow up 24-hour and exercising ECGs should be performed at least annually.

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